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SPECIFICATION

1. TITLE OF THE INVENTION

Soft capsule

2. SCOPE OF PATENT CLAIMS

(1) Soft capsule with pH of 5 or less and moisture content of 9% by weight or less.

3. DETAILED DESCRIPTION OF THE INVENTION

(INDUSTRIAL FIELD OF APPLICATION)

This invention relates to a soft capsule filled with pharmaceuticals or the like.

(PRIOR ART)

To facilitate ingestion of pharmaceuticals and the like and ensure that they are absorbed by the intended digestive organs, pharmaceuticals and the like are made into encapsulated formulations by being packed into soft capsules (also called "soft elastic capsules"). Soft capsules of this kind must have enough strength to maintain their shape and yet must also be able to disintegrate, and this ability to disintegrate must not decline over time.

This decline in the ability to disintegrate occurs due to insolubilization over time of the gelatin comprising the capsule. Decline in the ability of a capsule to disintegrate is particularly marked when the capsule contains fish liver oil or the like. Insolubilization is believed to occur when the gelatin reacts with the content.

A soft capsule that prevents this insolubilization of the gelatin has been disclosed in Japanese Unexamined Patent Application Publication S58-62120. This soft capsule is made by adding 0.5–10% by weight polypeptide to gelatin. Insolubilization is surmised to be prevented because the polypeptide reacts with the content before the gelatin, inhibiting the reaction with the gelatin.

In addition, a soft capsule with better disintegrating ability than prior-art soft capsules is disclosed in Japanese Examined Patent Application Publication S56-31981. This soft capsule is made by forming a film made of gelatin having a jelly strength of 60–120 bloom and viscosity of 22–35 mP. Restricting the gelatin to the aforesaid physical

properties improves the disintegrating ability of the soft capsule. The reason for this is surmised to be that gelatin with the aforesaid physical properties contains a comparatively larger number of polypeptides.

(PROBLEM TO BE SOLVED BY THE INVENTION)

However, a problem that has come to light with the soft capsules disclosed in the aforesaid unexamined patent application publication is that, if the content is a highly reactive substance, this increases the amount of polypeptides consumed by the reaction, resulting in an inadequate ability to prevent insolubilization within the aforesaid scope. Furthermore, if the amount of polypeptides added to the gelatin is increased in an attempt to overcome this problem, this results in the problem of decreasing the strength of the capsule.

In the case of the soft capsule disclosed in the aforesaid examined patent application publication as well, a problem is that if the content is a highly reactive substance, the gelatin becomes inadequately able to prevent insolubilization.

This invention was devised in view of this situation, and has as its objective to provide a soft capsule that can prevent insolubilization of the gelatin.

(MEANS FOR SOLVING THE PROBLEM)

To achieve the aforesaid objective, this invention is a soft capsule with pH of 5 or less and moisture content of 9% by weight or less.

Below is a detailed description of the invention.

The soft capsule in this invention has a pH of 5 or less and moisture of 9% by weight or less. If the soft capsule has a pH greater than 5 or moisture greater than 9% by weight, the effect of preventing insolubilization will be reduced.

There is no particular restriction on the method of making the soft capsule have a pH of 5 or less, but by way of example, this can be done by adding inorganic and/or organic acid or using low pH gelatin (for example, pH 5.0 or less), etc. Examples of the aforesaid inorganic acid that can be used include hydrochloric acid, sulfuric acid, etc., and examples of the aforesaid organic acid include phosphoric acid, etc. There is no particular restriction on the method of making the moisture of the soft capsule 9% by weight or less, but by way of example, this can be done by extending the drying time when manufacturing the soft capsule or increasing the drying temperature, etc. Regarding when the pH is to be adjusted, the pH can be adjusted when producing the soft capsule preparation fluid, or gelatin with the appropriate pH can be used, etc. There is no particular restriction on how to keep the soft capsule at a moisture content of 9% by weight or less, but by way of example, this can be done by storing it in a sealed container.

At the very least, gelatin is used in the soft capsule in this invention. In addition to gelatin, plasticizer, preservative, thickener, colorant, etc. may be added to the soft capsule in this invention as required, either singly or in combinations of two or more. Examples of the aforesaid plasticizer include glycerin and sorbitol, each of which can be used alone or in combinations of two or more. Examples of the aforesaid thickener include gum arabic and alginic acid, each of which can be used alone or in combinations of two or more. Examples of the aforesaid colorant include food colorant, each of which may be used alone or in combinations of two or more.

There is no restriction on the gelatin used in this invention.

If the pH of the soft capsule is restricted to within the aforesaid range, the jelly strength thereof may decline and the heat produced by dissolving/degassing during capsule manufacture may accelerate deterioration of the physical properties of the gelatin due to the pH-dependence of gelatin. In short, if the jelly strength of the gelatin goes below 200 bloom, there may be some instances when it will be difficult to prevent the strength thereof from decreasing when the pH of the soft capsule is made 5 or less. Furthermore, if the viscosity of the gelatin goes above 35 mP, this will slow down degassing when manufacturing the soft capsule, promoting heat degradation of the gelatin at a low pH, so there will be a tendency for the strength of the soft capsule to decline excessively.

In this case, in this invention, using gelatin with a jelly strength of 200 bloom or more and a viscosity of 35 mP or less will reduce the amount of time required for degassing when producing the capsule, which will make it possible to prevent heat degradation at a low pH. This will make it

possible to prevent insolubilization of the gelatin and yet also prevent impairment of capsule strength. Note that for the purposes here, jelly strength and viscosity are measured according to JIS-K-6503 (1977).

The soft capsule in this invention differs from prior-art soft capsules in that it has a low pH and moisture content, but the method and device used to manufacture the capsule can be the same as those used prior to now. Hence, there is no need to invest in new equipment to manufacture the soft capsule in this invention. For example, an aqueous solution containing gelatin and other components as needed can be prepared, and this aqueous solution can be dried by a conventional method and made into a sheet. Using this sheet, capsules can be manufactured by a continuous method such as filling content using a rotary filler. Alternately, using the aforesaid sheet, capsules can be manufactured by the flat plate method. Capsules can even be manufactured by a method such as the globex method, wherein the content is filled at the same time as the capsules are manufactured without forming a sheet ahead of time. There is no particular restriction on the method used to manufacture the soft capsule in this invention.

The soft capsule in this invention can be filled with any of various kinds of content including pharmaceuticals, food products and the like, without any particular restrictions. Also, the content is not restricted to content in the liquid form.

(OPERATION)

The pH and moisture content of the soft capsule in this invention are restricted to within the aforesaid range, which prevents the reactivity of the gelatin comprising the soft capsule from declining and thereby causing the disintegrating ability to decline over time, as well as preventing insolubilization of the gelatin over the long term even when the content is a highly reactive substance.

(EMBODIMENTS)

Embodiments of this invention will be described below in comparison with prior-art examples and comparative examples that deviate from the quantitative scope of this invention. However, this invention is not restricted to the embodiments.

(EMBODIMENTS AND COMPARATIVE EXAMPLES 1 & 2)

Soft capsule preparations were produced by thoroughly mixing the components in the formulations shown in Table 1 by heating until dissolved. Each preparation was then cooled into a sheet shape, from which soft capsule sheets were produced by drying at low heat. The pH of each sheet was measured and these are shown in Table 1. Note that the gelatin that was used had a jelly strength of 250 bloom and a viscosity of 31 mP.

The moisture content of each sheet was adjusted to the values shown in Table 1 by adjusting the drying time when the sheet was produced.

The disintegrating ability of each sheet was investigated. The disintegrating ability of each sheet was measured immediately after manufacture, after being stored at 40°C for 6 months, and after being stored at 20°C while immersed in fish liver oil for 1 month, by measuring the time it took to disintegrate in 37°C synthetic gastric juice using a disintegration tester. The disintegration time per 0.2 g of each sheet is shown in Table 1.

Table 1

		Embodiment	Comparative Ex. 1	Comparative Ex. 2
Composition of soft capsule preparation (g)	Gelatin	100	100	100
	Glycerin	40	40	40
	Water	260	260	260
	Acid or alkali used to adjust pH	HCl	None	HCl
pH of sheet		4.0	6.5	4.0
Moisture content of sheet (% by weight)		8.0	8.0	10.0
Disintegrating ability of sheet (minutes)	Immediately after manufacture	6.0	7.0	6.0
	6 months after manufacture	10	24	18
	After being immersed in liver oil for 1 month (stored at 20°C)	17	Insolubilized	Insolubilized

As indicated in Table 1, the sheet in the Embodiment underwent less decline in disintegrating ability over time in comparison with the sheets in Comparative Examples 1 and 2. Furthermore, despite having been immersed in liver oil for 1 month, the sheet in the Embodiment did not insolubilize, whereas the sheets in Comparative Examples 1 and 2 both insolubilized after being immersed in liver oil for 1 month.

(EFFECT OF THE INVENTION)

Because the soft capsule in this invention has a pH of 5 or less and moisture content of 9% by weight or less, it undergoes virtually no decline in disintegrating ability over time. Furthermore, the decline in disintegrating ability over time remains small even when in contact with a relatively highly reactive substance.

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